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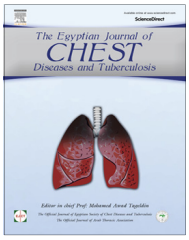

ORIGINAL ARTICLE

Iron deficiency anemia as a risk factor in childhood asthma

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KEYWORDS

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Abstract *Aim of the work:* To assess iron deficiency anemia as a risk factor for childhood asthma and its possible effect on pulmonary functions.

Patients and methods: Cohort prospective study was carried out on 100 children, 6–16 year olds who attended the outpatient pediatric clinic, Benha University hospital with upper or lower respiratory tract infection, from May 2011 to May 2012, after getting concent from their parents, they were classified into: group I: 50 children with iron deficiency anemia, subdivided into group Ia: asthmatic children and group Ib: non asthmatic children. Group II: 50 children without iron deficiency anemia, subdivided into group IIa: asthmatic children and group IIb: non-asthmatic children. All patients were subjected to full history taking and physical examination, complete blood count, serum ferritin level, liver and kidney function tests, Plain Chest X-ray P-A view and pulmonary function tests.

Results: There was no statistically significant difference between the two groups regarding age and BMI, but a significant difference regarding sex. There was a significant difference between the two groups regarding the number of asthmatics as they were more in group I. There was a significant positive correlation between hemoglobin level and pulmonary function parameters (FEV1, FVC, FEV1/FVC, PEF) in (group Ia). There was a significant positive correlation between

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serum ferritin level and pulmonary function parameters (FEV1, FVC, FEV1/FVC, PEF) in group Ia however there was no significant correlation between serum ferritin and post-bronchodilators changes in FEV1. There was a statistical significant difference between the anemic group and non-anemic group regarding PFTs as PFTs were better in non-anemic group.

Conclusions: Iron deficiency anemia may be considered as an indirect risk factor for childhood asthma also iron deficiency anemia may have a negative effect on spirometry of asthmatic children.

Introduction

Asthma is a common medical problem encountered by clinicians dealing with children. Its incidence has substantially increased worldwide [1]. Asthma is a chronic inflammatory disorder of air ways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing particularly at night or in the early morning. These episodes are usually associated with wide spread but variable airflow obstruction within the lung that is often reversible either spontaneously or with treatment [2].

Exacerbations of asthma (asthma attacks or acute asthma) are episodes of a progressive increase in shortness of breath, cough, wheezing, or chest tightness, or some combination of these symptoms. It is a chronic inflammatory condition of the lung airways resulting in episodic airflow obstruction [3].

Anemia associated with acute infections occurs more commonly in children than in adults. Anemia exerts adverse effects on immune response and alters the metabolism and growth of pathogens. It has already been reported that low hemoglobin impaired tissue oxygenation and acts as an independent risk factor for developing lower respiratory tract infections (LRTI) in children [4].

Aim of the work

The aim of this study was to investigate iron deficiency anemia as a risk factor for childhood asthma and its possible effect on pulmonary functions.

Subjects and methods

This cohort prospective study was carried out on 100 children in the age group of 6–16 years who attended the outpatient pediatric clinic Benha University hospital with upper or lower respiratory tract infection, 50 patients with IDA and 50 children without IDA and they were examined and investigated for diagnosis of bronchial asthma in the period from May 2011 to May 2012, after an oral concept of their parents, they were classified into:

- Group I: 50 children with iron deficiency anemia that was subdivided into:
  - Group Ia: asthmatic children
  - Group Ib: non asthmatic children
- Group II: 50 children without iron deficiency anemia that was subdivided into:
  - Group IIa: asthmatic children
  - Group IIb: non-asthmatic children

Inclusion criteria

A. Criteria for diagnosis of bronchial asthma in children [17–19]:
1. A history of intermittent or chronic symptoms typical of asthma.
2. The finding on physical examination of characteristic musical wheezing (present in association with symptoms and absent when symptoms resolve).
3. Confirmation of the diagnosis of asthma is based on two key additional elements
   - The demonstration of variable expiratory airflow limitation by spirometry (post-bronchodilator changes in FEV1 $\geqslant$ 8).
   - Exclusion of alternative diagnoses.

B. Criteria for diagnosis of anemic children:The child considered to be anemic if serum ferritin level <12 μg/dl. The normal range is (l5–300 μg/dl) [5].

Exclusion criteria

- Anemia other than iron deficiency anemia.
- Chronic chest disease other than bronchial asthma.
- Heart disease.
- Liver disease.
- Kidney disease.

All patients were subjected to:

I. Full history taking and physical examination:With special attention to intermittent attacks, Cough and expectoration, Wheezy dyspnea and Chest tightness, Tachypnea, Signs of hyperinflation, prolonged expiratory phase, Expiratory Rhonchi and pallor.

II. Laboratory investigations:
   - Complete blood count.
   - Serum ferritin level.
   - Kidney function tests.
   - Liver function tests

III. Plain Chest X-ray P-A view:The chest radiograph was done to exclude other causes of wheezing other than asthma including congenital malformations (e.g. right

aortic arch suggestive of a vascular ring); evidence of air-space disease consistent with aspiration or cystic fibrosis; or findings suggestive of asthma, such as hyperinflation, peribronchial thickening, and mucoid impaction with atelectasis.

IV. Ventilatory function tests (spirometry) before and after bronchodilatation by using Sensor-medics V max series, 2130 spirometer, V6200 Autobox, 6200DL. All results were calculated as percent of predicted except for FEV1/FVC.

Statistical analysis

Data were analyzed using SPSS (Statistical Package for Social Sciences) version 15. Qualitative data were presented as number and percent. Comparison between groups was done by Chi-Square test. Quantitative data were presented as mean ± SD. Student's *t*-test was used to compare between two groups. Pearson's correlation coefficient was used to test correlation between variables. $P < 0.05$ was considered to be statistically significant [6].

Results

The results are shown in Tables 1–7.

Discussion

Asthma affects an estimated 300 million individuals worldwide. Annually, the World Health Organization (WHO) has estimated that 15 million disability-adjusted life-years are lost and 250,000 asthma deaths are reported worldwide [7]. Anemia and respiratory tract infections are common problems among primary school children of low socioeconomic status, and a complex relation exists between iron status and infection. Iron deficiency and anemia are associated with impaired immunocompetence and the increased morbidity [8]. In the current study the age of group I ranged from 6 to 16 years and mean was 10.2 ± 3.1 and in group II their ages ranged from 6 to 16 years and mean was 10.9 ± 3.2. The study showed no statistical significant difference between group I and group II regarding age ($P > 0.05$) (Table 1).

In the current study group I included 34 males and 16 females (68:32)% and group II included 29 males and 21 females (58:42)%. The study showed that there was statistical significant difference between group I and group II regarding sex distribution ($p < 0.05$) as male sex was significantly higher in group I (Table 2).

In the present study the BMI in group I ranged from 22 to 30 and mean was 25.6 ± 8.9 and in group II the BMI ranged from 21 to 29 and mean was 24.8 ± 7.3. The study showed that there was no significant statistical difference between the studied groups with *P* value > 0.05 (Table 3).

In this study there were 33 asthmatic children (66%) in group I and 12 asthmatic children (24%) in group II. The study showed that there was a high statistical significant difference between the two groups regarding the presence of asthma that was significantly higher in group I (Table 4) this result was in accordance with that of Ramakrishnan and Ashwin Borade [9] who studied anemia as a risk factor for childhood asthma, their study included 200 children in the age group of 2–18 years with upper or lower respiratory tract infection, 100 children with anemia were taken as the study group and another 100, age and sex matched children without anemia were taken as the control PFT_S were performed on those above 6 years showing evidence of asthma and the study showed that anemic children were 5.75 times more susceptible to asthmatic attacks when compared with non anemic children, and they stated that the increased incidence of asthmatic attacks in anemic children may be due to the following facts: Hb facilitates oxygen (O_2) and carbon dioxide transport. It carries and inactivates nitric oxide (NO) and plays the role of the buffer [10]. Hemoglobin in the blood is mainly responsible for stabilizing the oxygen pressure in the tissues [11]. Qualitative and/or quantitative reduction in Hb may adversely affect the normal functions. Another study by Elizabeth et al. [12] who studied association of maternal anemia with increased wheeze and asthma in children. Their study included 597 families who had previously participated in the Asthma in Pregnancy (AIP) Study, the study showed that women with maternal anemia were more likely to have infants with recurrent wheeze in the first year of life compared to mothers without anemia (OR = 2.52, 95% CI 1.50, 4.23); similarly, odds of wheezing before age of 3 years among children born to mothers with anemia was significantly elevated compared to non-anemic mothers (OR = 2.44, 95% CI 1.48, 4.04).

Table 1 Age distribution among the studied groups.

Variable	Groups	Range	Mean ± SD	*P* value	Significant
Age	Group I	6–16	10.2 ± 3.1	>0.05	NS
	Group II	6–16	10.9 ± 3.2		

This table shows that there is no statistically significant difference between group I and group II regarding age ($P > 0.05$).

Table 2 Sex distribution among the studied groups.

Sex	Group I		Group II		*P* value	Significant
	No	%	No	%		
Male	34	68	29	58	$p < 0.05$	S
Female	16	32	21	42		
Total No	50		50			

This table shows that there is a statistically significant difference between group I and group II regarding sex ($p < 0.05$) as anemia was more common in males than females.

Table 3 BMI distribution among the studied groups.

Variable	Groups	Range	Mean ± SD	*P* value	Significant
BMI	Group I	22–30	25.6 ± 8.9	>0.05	NS
	Group II	21–29	24.8 ± 7.3		

This table shows that there is no statistical significant difference between group I and group II regarding BMI ($P > 0.05$).

Table 4 Statistical comparison between anemic and non-anemic groups regarding asthmatic cases.

Asthmatic cases	Anemic group No = 50		Non anemic group No = 50		*P* (odd ratio)	Sig
	NO	%	NO	%		
Yes	33	66	12	24	< 0.01 (3.1)	HS
No	17	34	38	76		

This table shows that there was a significant difference between two groups regarding the presence of asthma as bronchial asthma was more prevalent in the anemic group.

Table 5 Statistical correlation between hemoglobin and pulmonary function parameters in anemic asthmatic group (Ia).

HB/pulmonary function	*r*	*P*
FVC	0.418	< 0.01
FEV_1	0.478	< 0.01
FEV_1/FVC	0.335	< 0.01
PEF	0.401	< 0.01

This table shows that there is a statistically significant positive correlation between hemoglobin level and FVC, FEV1, FEV_1/FVC, and PEF in-group Ia.

Table 6 Statistical correlation between ferritin and pulmonary function parameters in anemic asthmatic group (Ia).

Ferritin/pulmonary function	*r*	*P*
FVC	0.512	< 0.01
FEV_1	0.517	< 0.01
FEV_1/FVC	0.395	< 0.01
PEF	0.497	< 0.01
Post bronchodilator changes in FEV_1	0.079	> 0.05

This table shows that there is a statistically significant positive correlation between serum ferritin level and FVC, FEV1, FEV_1/FVC, and PEF in-group Ia. In addition, these was non significant statistical correlation between serum ferritin level and post bronchodilator changes in FEV_1.

Maternal anemia was also associated with their child's asthma; mothers that were anemic during pregnancy were more likely to have a child ever diagnosed with asthma (OR = 2.37, 95% CI 1.39, 4.03), and a child with asthma at age 6 (OR = 2.64, 95% CI 1.54, 4.53) than non-anemic women. Also the study showed that 12% of mothers had anemia while pregnant. Among their children, 22% had recurrent wheeze in the first year of life and 17% had active asthma at age six.

Also this result was in agreement with that of Sleem et al. [13] who studied the effect of both antileukotriene therapy and mild dose theophylline as controller therapy added to low dose ICS compared with moderate dose ICS on asthmatic patients who are poorly controlled on low dose ICS. Their study included 45 Egyptian children with mild to moderate persistent asthma and followed up for a 3 month treatment in chest hospital in Benha. There were 28 males and 17 females. Their ages ranged from 5 to 15 years with a mean age of 7.5 ± 3.1 years. After the 3 month treatment, the study showed that hemoglobin levels were low in most asthmatic children.In the present study there was a significant positive correlation between HB level and pulmonary function tests in anemic asthmatic group Ia (Table 5).In this study there was a significant positive correlation between serum ferritin level and FVC, FEV, FEV_1/EVC & PEF and non statistical significant positive correlation between serum ferritin level and post bronchodilator changes in FEV_1 in anemic asthmatic (group Ia) (Table 6).In this study there was a statistical significant difference between group Ia and group IIa regarding pulmonary function parameters ($P > 0.05$) that was significantly higher in group IIa (Table 7). Pulmonary function tests provide valuable information about the status of an individual's respiratory system and work capacity [14]. Various studies have shown deleterious effect of anemia on various systems of the body like involvement of nervous system leading to insomnia, mental irritation, lightheadedness, impaired cognitive functions etc. It also affects the immune system of the body and reduces immunity. A decrease in strength of respiratory muscles including diaphragm reduces the pulmonary functions [15]. Tidal volume is decreased while reserve volumes increase or remain unchanged in these anemic persons. However total lung capacity markedly decreases in these subjects suffering from anemia. Weakness of accessory muscles of respiration adds to a decrease in Peak expiratory flow rate, forced expiratory volume in one second (FEV1). Maximum voluntary ventilation is markedly reduced due to the decreased

Table 7 Statistical comparison between group (Ia) and (IIa) regarding pulmonary functions.

Group		FVC	FEV_1	FEV_1/FVC
GROUP (Ia)	Range	(54–75)	(54–78)	(56–67)
No = 33	Mean + SD	64.2 ± 11.5	58.5 ± 8.3	53.3 ± 10.0
Anemic asthmatic				
GROUP (IIa)	Range	(65–78)	(59–79)	(52–65)
No = 12	Mean + SD	72.0 ± 9.4	65.0 ± 7.4	60.6 ± 9.0
Non anemic asthmatic				
t		2.3	2.5	2.3
p		< 0.05	< 0.05	< 0.05

This table shows that there is a statistically significant difference between group Ia and group IIa regarding pulmonary function parameters) FVC, EEV_1, FEV_1/FVC) ($P > 0.05$) as it was better in-group IIa.

depth of respiration as well. Anemia leads to decreased pulmonary functions which further hampers the oxygenation of the tissue and may worsen the physical and mental capabilities [16].

Conclusion

- Iron deficiency anemia may be considered as an indirect risk factor for development of asthmatic attacks in children.
- Iron deficiency anemia may have a negative effect on spirometry in asthmatic children that may lead to an increased severity of asthmatic attacks.

Conflict of interest

No conflict of interest.

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